Attoreny Ref. 04676.105047 U.S.S.N. 09/436,892 Marked-Up Version

## Marked-Up Version of Original Claims

Claims 1, 2, 4-6, 9, 10 and 15 have been amended as follows:

- 1. (Amended) A method to assess whether a compound enhances the clearing of a is an LDL clearance enhancing drug that includes mixing the drug with cholesterol-containing low-density lipoprotein in a host human or animal comprising in vivo or in vitro; isolating the complex, and determining whether the binding of the compound to the complex causes a change in the three dimensional conformation of apoB-100 in the lipoprotein that enhances the binding affinity of the lipoprotein to the LDL receptor; wherein the LDL clearance enhancing drug is not probucol or a mono- or di-ester of probucol, not a compound described in WO 98/09773, and not a silyl compound described in U.S. Patent Nos. 5,155,250 or 5,608,095.
  - (a) administering the compound to the host;
  - (b) isolating cholesterol-containing low density lipoprotein from the host,
  - (c) determining whether the compound has bound to the cholesterolcontaining lipoprotein to form a complex; and
  - (d) determining whether the complex causes a change in the three

    dimensional conformation of the lipoprotein that enhances the
    binding affinity of the lipoprotein to the LDL receptor.
- 2. (Amended) The method of claim 1, wherein the eholesterol-containing lipoprotein is LDL compound changes the conformation of apolipoprotein in the low density lipoprotein (LDL).
- 4. (Amended) The method of claim 1, wherein the binding of the compound to the complex is determined assessed by a sandwich ELISA.
- 5. (Amended) The method of claim 1, wherein the binding of the compound to the complex is determined assessed using agarose electrophoresis.
- 6. (Amended) A method to alter the conformation of a cholesterol-containing lipoprotein comprising mixing the cholesterol-containing lipoprotein in vivo or in vitro with a compound and

determining whether the binding of the compound to the complex causes a change in the three dimensional conformation of apoB-100 in the lipoprotein that enhances the binding affinity of the lipoprotein to an LDL receptor determine whether a compound will increase the clearance of a low density lipoprotein in a host, comprising

- (i) mixing the compound with low density lipoprotein;
- (ii) determining whether the compound and the low density lipoprotein form a complex; and
- (iii) determining whether the complex alters the three dimensional conformation of the lipoprotein such that the binding of the lipoprotein to a lipoprotein receptor is enhanced.
- 9. (Amended) A method to determine if a compound causes a change in the structure of apoB-100 apolipoprotein B-100 in a cholesterol-containing low density lipoprotein that would be therapeutically useful, comprising: earrying out a sandwich immunoreactivity assay in which an antibody directed to an epitope on apoB-100 (known to be important to the LDL receptor binding process) as a capture antibody is laid onto a plate, the cholesterol containing lipoprotein/test compound complex is added to the plate, and a second antibody, which can be polyclonal or monoclonal, is then used to quantify the amount of LDL complex captured.

## (i) mixing the compound with low density lipoprotein;

- (ii) carrying out a sandwich immunoreactivity assay on the compound low density lipoprotein mixture using an antibody directed to the epitope on apolipoprotein B-100 that binds to the LDL-receptor,
- (iii) using a second antibody to quantify the amount of LDL captured by the assay; and
  - (iv) comparing the amount of LDL captured by the assay to a control.
- 10. (Amended) A method The method of claim 6, wherein, the to assess a conformational change in a cholesterol containing lipoprotein-is assessed by observing a caused by complexation with a test compound comprising assessing the change in the electrophorectic mobility pattern of the cholesterol-containing lipoprotein using electrophoresis.

- 15. (Amended) A method for assessing whether a compound binds to a lipoprotein in a manner which lowers plasma cholesterol comprising complexing the compound with cholesterol containing lipoprotein, isolating the resulting complex, and determining whether the binding of the compound to the complex causes a change in the three dimensional conformation of apoB-100 in the lipoprotein that enhances the binding affinity of the lipoprotein to the LDL receptor enhances the binding of the lipoprotein to a lipoprotein receptor and thus lowers plasma cholesterol, the method comprising:
- (a) allowing the compound to form a complex with a cholesterol-containing lipoprotein in vivo,
  - (b) isolating the resulting complex, and
- (c) determining whether the formation of the complex causes a change in the three dimensional conformation of apoB-100 in the lipoprotein that enhances the binding of the lipoprotein to the LDL hepatic receptor.